REMARKS

This Amendment is in response to the non-final Office Action dated April 25, 2007. The Office Action set a statutory period for response of three months. Applicants have submitted a petition for extension of time to file a response to October 25, 2007. Accordingly, this response is timely filed by October 25, 2007. The following remarks are respectfully submitted to place the application in condition for allowance.

1. Summary of Claims

A detailed listing of all claims that are, or were, in the application, irrespective of whether the claims remain under examination in the application, is presented, with an appropriate defined status identifier. Claims 1-65, 70-71, 77-78, 81 and 83-114 were previously cancelled.

By this amendment, Applicants have amended claims 66-69, 72-74, 82, 116, 123-125, 127-128, 130-131, 137, 140, 147-149, 151-152, 154-155, 158-161. Applicants have cancelled claims 75-76, 79-80, 129, 132-133, 153 and 156-157. Also, Applicants have added claims 163-171.

The subject application is a continuation of U.S. Serial No. 10/346,853, filed January 17, 2003, which is a continuation of U.S. Serial No. 09/100,812, filed June 19, 1998 (the "'812 Application"), now U.S. Patent No. 6,573,099, issued June 3, 2003, which claims priority of Australian Provisional Patent Application No. PP2492, filed March 20, 1998 (the "Priority Application").

Support for the amendment to claims 66 and 67 can be found, *inter alia*, at page 16, lines 20 to 26, page 8, lines 14 to 22, page 18, lines 11 to 20, page 19, lines 14 to 22, page 22,

lines 12 to 21 and page 11, lines 28 to 30 of each of the subject application, the '812 Application and the Priority Application.

Support for the amendment to each of claims 68, 69 and 72 can be found, *inter alia*, at page 16, lines 20 to 26 of each of the subject application, the '812 Application and the Priority Application.

Support for the amendment to each of claims 73 and 74 can be found, *inter alia*, at page 16, lines 20 to 26, page 8, lines 14 to 22 and page 10, lines 10 to 13 of each of the subject application, the '812 Application and the Priority Application.

Support for the amendment to each of claims 116 and 140 can be found, *inter alia*, at page 16, lines 20 to 26, page 7, lines 22 to 25 and page 10, lines 15 to 17 of each of the subject application, the '812 Application and the Priority Application.

Support for the amendment to each of claims 123, 124, 147 and 148 can be found, *inter alia*, at page 16, lines 20 to 26, page 6, lines 17 to 22 and page 12 lines 1 to 4 of each of the subject application, the '812 Application and the Priority Application.

Support for the amendment to each of claims 125, 149 and 151 can be found, *inter alia*, at page 12, lines 1 to 4 and page 19, line 28 to page 20 line 5 of each of the subject application, the '812 Application and the Priority Application.

Support for the amendment to each of claims 128 and 152 can be found, *inter alia*, at page 16, lines 20 to 26 and page 17, lines 14 to 22 of each of the subject application, the '812 Application and the Priority Application.

Support for the amendment to each of claims 130, 131, 154 and 155 can be found, *inter alia*, at page 16, lines 20 to 26 and page 18, lines 11 to 20 of each of the subject application, the '812 Application and the Priority Application.

Support for the amendment to claim 158 can be found, *inter alia*, at page 4, lines 3 to 4, page 23, lines 23 to 24 and page 24, lines 23 to 24 of each of the subject application, the '812 Application and the Priority Application.

Support for the amendment to claim 159 can be found, *inter alia*, at page 16, lines 20 to 26 and page 12, line 6 to page 14, line 9 of each of the subject application, the '812 Application and the Priority Application.

Support for the amendment to claim 160 can be found, *inter alia*, at page 13, lines 19 to 22 of each of the subject application, the '812 Application and the Priority Application.

Support for the amendment to claim 161 can be found, *inter alia*, at page 22, lines 16 to 19 of each of the subject application, the '812 Application and the Priority Application.

Support for new claim 163 can be found, *inter alia*, at page 10, lines 15 to 21, page 16, lines 20 to 26, page 8, lines 14 to 22, page 18, lines 11 to 20, page 19, lines 14 to 22, page 22, lines 12 to 21 and page 11, lines 28 to 30 of each of the subject application, the '812 Application and the Priority Application.

Support for new claim 164 can be found, *inter alia*, at page 11, lines 20 to 30 of each of the subject application, the '812 Application and the Priority Application.

Support for new claim 165 can be found, *inter alia*, at page 1, lines 5 to 9, page 4, lines 3 to 4 and page 12, line 20 of each of the subject application, the '812 Application and the Priority Application.

Support for new claims 166 to 171 can be found, *inter alia*, at page 2, lines 5 to 9, page 11, line 28 to page 14, line 9, page 16, lines 12 to 18, page 21, lines 26 to 29, page 23, lines 9 to 15 and page 24, lines 26 to 29 of each of the subject application, the '812 Application and the Priority Application.

No new matter has been added by these amendments. Applicants respectfully request entry of the amended and new claims in the present application.

2. Election/Restriction

Applicants submit that there are generic and linking claims in the present invention. As the Examiner stated in the Requirement for Restriction dated July 31, 2006, upon allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 C.F.R. § 1.141.

By this Amendment, Applicants have added new claims 163 – 170. Applicants submit that each of the new claims is readable on the elected species of a target gene from a ssRNA virus.

3. Priority Under 35 U.S.C. § 120

The Examiner noted that the oath incorrectly lists the priority document as PP2292, which should be PP2492. The correct priority application number is PP2492. Applicants submitted a claim of priority in the '812 Application correcting the reference to the PP2492 application. The typographical error was also corrected in a subsequent declaration filed in the related application 09/646,807 filed under 35 U.S.C. § 371, which is attached as **Exhibit A** to this response.

"Priority" Under 35 U.S.C. § 120 – Written Description Requirement for claims 66-69, 72-74, 82, 115-119, 121, 123-143, 145 and 147-162

The Examiner asserted that Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 120. Specifically, the Examiner stated that the disclosure of the invention in the parent application and in the later- filed application do not comply with the requirements of the first paragraph of 35 U.S.C. § 112, citing *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). The Examiner alleged that the disclosure of the prior-filed application, Application No. 09/100,812 (Patent No. 6,573,099), fails to provide adequate support or enablement for instant claims 66-69, 72-74, 82, 115-119, 121, 123-143, 145 and 147-162 "under 112 first paragraph for a genus of. The specification...." The Office Action does not state the genus and it is not clear what the Examiner intended to specify as the genus. The Examiner continued by stating "[t]he specification of '812 contemplates: 'at least about 20-30 nucleotides in length derived from a viral DNA polymerase, viral RNA polymerase...' and 'the structural gene component....'" Applicants presume the Examiner meant to specify a genus of target genes or structural genes and respond accordingly. If this was not what the Examiner intended, then Applicants request that the Examiner explain in more detail and thereby give Applicants an opportunity to address such rejection before making any action final.

Applicant's Response

Applicants respectfully traverse the alleged suggestion the '812 Application fails to support the currently amended claimed invention under 35 U.S.C. § 120. M.P.E.P. § 2163 indicates that "[t]o satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably

conclude that the inventor had possession of the claimed invention." (emphasis added; citations omitted). Applicants maintain that each of the priority applications satisfies this requirement.

Applicants point to the disclosure in each of the present application, the '812 Application and the priority application PP2492 at page 8, lines 14 to 22 for the teaching of the feature "nucleotide sequence is substantially identical to at least a sequence of a target gene in an animal cell". It is clear from these passages that the disclosure of the "at least a sequence of a target gene" is in the context of any target gene in the animal cell, *i.e.,* it is not limited to the species of target gene "viral DNA polymerase, viral RNA polymerase..." as referred to by the Examiner (Office Action, page 4). The disclosure in each application also provides specific definitions at page 7 lines 1 to 20 of the terms synthetic gene, structural gene sequence, and target gene. Moreover, page 7, line 5 of the application discloses that the term "structural gene" refers to a nucleotide sequence. The Examiner alleged that the specification of the '812 Application does provide written support for a genus of "structural gene." Without conceding the correctness of the Examiner's position and to expedite prosecution, Applicants have amended the claims to recite "nucleotide sequence."

The Examiner stated "The skilled artisan cannot envision the detailed structure of a genus of structural genes that must exhibit the contemplated biological functions." (page 5). In response, without conceding the correctness of the Examiner's position and to expedite prosecution, Applicants have amended the pending claims to no longer recite the functional language to which the April 25, 2007 Office Action objected.

For completeness of the record, in regard to amended claims 66 and 67:

the element "synthetic genetic construct" is described, *inter alia*, at page 2, line 28, page 3, lines 27 to 30, page 23, lines 10 to 19 and page 24 lines 21 to 24 of each of the subject application, the '812 Application and the Priority Application;

the element "two identical nucleotide sequences" is described, *inter alia*, at page 16, lines 20 to 26 of each of the subject application, the '812 Application and the Priority Application;

the element "substantially identical" is described, *inter alia*, at page 8, lines 17 to 22 of each of the subject application, the '812 Application and the Priority Application;

the element "target gene" is described, *inter alia*, at page 7, lines 17 to 20 of each of the subject application, the '812 Application and the Priority Application;

the element "animal cell" is described, *inter alia*, at page 1, lines 5 to 7 and page 12, lines 18 to 20 of each of the subject application, the '812 Application and the Priority Application;

each of the elements "head-to-head," "tail-to-tail" "configuration" and "relative to each other" are described, *inter alia*, at page 18, lines 11 to 14 of subject application, the '812 Application and the Priority Application.

the elements "spatially separated," "linked", "stuffer fragment" and "sequence of nucleotides" is described, *inter alia*, at page 19, lines 14 to 19 of subject application, the '812 Application and the Priority Application.

the element "placed" is described, *inter alia*, at page 12, lines 28 and 29 of subject application, the '812 Application and the Priority Application;

the element "operably under the control" is described, *inter alia*, at page 14, lines 6 to 9 of subject application, the '812 Application and the Priority Application;

the element "single promoter sequence" is described, *inter alia*, at page 3, lines 9 to 16 of subject application, the '812 Application and the Priority Application, and page 16, lines 12 to 18 of subject application, the '812 Application and the Priority Application;

the element "transcription termination sequence" is described, *inter alia*, at page 22, lines 12 to 14 of subject application, the '812 Application and the Priority Application;

the element "which is active in the cell" is described, *inter alia*, at page 22, lines 19 to 21 of subject application, the '812 Application and the Priority Application;

the element "sense orientation" is described, *inter alia*, at page 11, line 28 to page 12, line 1 of subject application, the '812 Application and the Priority Application;

In regard to new claim 163:

Each of the elements "20-30 consecutive nucleotides", "a viral DNA polymerase," "viral RNA polymerase," "viral coat protein," "visually-detectable gene," is described at page 10, lines 15 to 21 and page 7, lines 22 to 25 of each of the subject application, the '812 Application and the Priority Application; and

the element "animal cell" is described, *inter alia*, at page 1, lines 5 to 7 and page 12, lines 18 to 20 of each of the subject application, the '812 Application and the Priority Application.

Applicants note that the Examiner has acknowledged on page 4 of the April 25, 2007 Office Action that the subject matter of new claim 163 is contemplated by the '812 Application. Therefore, new claim 163 and claims dependent thereon are understood not to be subject to this written description rejection.

In regard to each of amended claims 73 and 74, the element "30 contiguous nucleotides" is described, *inter alia*, at page 8, lines 17 to 22 and page 10, lines 10 to 13 of each of the subject application, the '812 Application and the Priority Application.

In regard to each of amended claims 116 and 140, the elements "a viral DNA polymerase," "viral RNA polymerase," "viral coat protein," are described at page 7, lines 22 to 25 of each of the subject application, the '812 Application and the Priority Application.

In regard to each of amended claim 128 and claim 152, the element "no more than 0.5-2.0kb" is described, *inter alia*, at page 17, lines 14 to 22 of each of the subject application, the '812 Application and the Priority Application.

In summary, each of the elements of the pending claims are described and/or defined in each of the subject application, the '812 Application and the Priority Application. Applicants therefore maintain that each of the subject specification, the '812 Application and the Priority Application fully describe the claimed invention, as required by M.P.E.P. § 2163.

Applicants respectfully submit that the amended claims have written description in each of the prior applications.

"Priority" Under 35 U.S.C. § 120 – Written Description Requirement for claims 128, 129, 152 and 153

The Examiner alleged that claims 128 and 152 did not have written support for the limitation 'no more than 2.0 kilobases' and claims 129 and 153 did not have written support for the limitation 'no more than 0.5 kilobases (kb).' The Examiner alleged that it appears that the only support for the limitations is on page 17, lines 20-22. The Examiner alleged that "on page 17, the support is for no more than 0.5-2.0 kb, not no more than either 0.5kb or 2.0kb with no lower limit." The Examiner alleged that thus, it appears that the specification only provides support for no more than 0.5-2.0 kb not below 0.5kb. (Office Action at page 6).

Applicants' Response

In response, without conceding the correctness of the Examiner's position and to expedite prosecution, Applicants have amended claims 128 and 152 to recite the limitation "no more than 0.5-2.0 kilobases," and have canceled claims 129 and 153.

In regard to claims 128 and 152, the element "no more than 0.5-2.0 kb" is described, *inter alia*, at page 17, lines 14 to 22 of each of the subject application, '812 Application and priority application PP2492.

Accordingly, Applicants maintain that the subject application complies with all requirements of 35 U.S.C. § 120, including 35 U.S.C. § 112, and respectfully request that the Examiner acknowledge Applicants' benefit claim under 35 U.S.C. § 120.

4. Claim Rejections Under 35 U.S.C. § 112

Rejection Under 35 U.S.C. § 112, First Paragraph – Written Description Requirement for claims 127, 128, 129, 151, 152 and 153

The Examiner rejected Claims 127, 128, 129, 151, 152 and 153 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner asserted that the disclosure does not provide support for the limitation 'no more than 2.0 kilobases' in claims 128 and 152 and the limitation 'no more than 0.5 kilobases (kb)' in claims 129 and 153. This rejection is substantially similar to the rejection above. The Examiner further asserted that the disclosure does not seem to provide support for the limitation "the stuffer fragment comprises an intron" in claims 127 and 151. The Examiner alleged New Matter.

Applicants' Response

In response, without conceding the correctness of the Examiner's position and to expedite prosecution, Applicants have amended claims 127, 128, 151 and 152 and have canceled claims 129 and 153.

In regard to each of amended claims 128 and 152, the element "no more than 0.5-2.0kb" is described, *inter alia*, at page 17, lines 14 to 22 of the subject application. In regard to each of the amended claims 127 and 151, the element "the stuffer fragment is an intron sequence" is described, *inter alia*, at page 19, line 29.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 127, 128, 151 and 152 under 35 U.S.C. § 112, first paragraph.

Rejections Under 35 U.S.C. § 112, First Paragraph – Written Description Requirement for claims 66-69, 72-74, 82, 115-119, 121, 123-143, 145 and 147-162

The Examiner rejected claims 66-69, 72-74, 82, 115-119, 121, 123-143, 145 and 147-162 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner alleged that the claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (Office Action at page 6).

The Examiner alleged that the instant claims are broadly drawn and read on a synthetic construct which is capable of delaying, repressing or otherwise reducing the expression of a target gene in an animal cell. The Examiner alleged that the broadest claims are not limited to any particular target genes from any particular organisms, reading on a large number of dsRNAs that are made that are substantially identical to at least any portion of any selected target gene from any source, that will function, as an [sic] dsRNA, to modulate gene expression. The Examiner asserted that in view of the elected species, the claims read on a genus of target genes encoding RNA polymerase from a genus of ssRNA viruses.

The Examiner alleged that the specification as filed does not provide an adequate written description of the vast genus of dsRNAs that are substantially identical to at least any portion of any selected target gene, that will function, commensurate with the breadth of what

is claimed, as siRNAs to reduced duplex stability, to modulate (reduce or induce, for example) the expression of any target RNA molecule.

The Examiner alleged that the specification as filed provides description or limiting definition of what is encompassed by substantial identity to a portion of a selected target gene or what it means to be substantially identical to a portion of a selected target gene. The Examiner alleged that the specification as filed provides description or limiting definition of what is encompassed by a portion of a selected target gene. The Examiner alleged that as discussed above under the priority section, the instant specification provides a general description of (pages 7-11) wherein it discloses that they are those dsRNAs that are effective in achieving modulation or attenuation of gene expression. The Examiner alleged that the specification discloses minimal examples of methods of making dsRNAs as claimed (page 25-39). (Office Action at page 8).

The Examiner alleged that therefore, in disclosing only broad and general guidance in regards to what is claimed, which is a method of making a dsRNA that is substantially identical to at least any portion of any selected target gene, that will function, commensurate with the breadth of what is claimed, as dsRNAs to modulate (reduce or induce, for example) the expression of that selected target gene and only limited examples of the claimed dsRNAs, the specification does not provide a representative number of species of the method of making, as claimed, that would be sufficient to show possession of the vast genus of methods now claimed. (Office Action at pages 8-9).

Applicants' Response

In response, Applicants respectfully traverse the rejection. To advance prosecution, however, Applicants have amended the pending claims to no longer recite the functional

language to which the April 25, 2007 Office Action objected. The rejection is therefore believed to be moot.

For the record, however, as discussed above, M.P.E.P. § 2163 indicates that "[t]o satisfy the written description requirement, a patent specification must describe the claimed invention in *sufficient detail* that one skilled in the art can *reasonably conclude* that the inventor had possession of the claimed invention." (emphasis added; citations omitted). The specification of the subject application describes in sufficient detail the characteristics of the two identical nucleotide sequences recited in the claims. Upon selecting a target gene, one of ordinary skill in the art using no more than general knowledge in the art would readily contemplate the identical nucleotide sequences within the metes and bounds of the now pending claims.

There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) ("we are of the opinion that the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims"). M.P.E.P. § 2163.

The invention claimed in amended claim 66 is a synthetic genetic construct which comprises two identical nucleotide sequences each of which is substantially identical to a target gene in an animal cell, wherein the two identical nucleotide sequences are oriented in a head-to-head, head-to-tail or tail-to-tail configuration relative to each other and are spatially separated and linked by a stuffer fragment which comprises nucleotides. The two identical nucleotide sequences and stuffer fragment are placed operably under the control of a single promoter sequence and a transcription termination sequences. The claimed invention is supported in the specification for making the synthetic genetic construct using a nucleic acid

sequence that is highly specific to a target gene in an animal cell.

The Examiner asserts that "the specification as filed does not provide an adequate written description of the vast genus of dsRNAs that are substantially identical to at least any portion of any selected target gene...." The application provides specific definitions at pages 6-7 of the terms gene, synthetic gene, and target gene. Page 7 line 1 teaches that the structural gene shall be taken to refer to a nucleotide sequence. Page 8 lines 14 to 22 and page 10 lines 10 to 13 define the term "substantial identity" and describe the relationship of the one or more copies of the nucleotide sequence of the claimed synthetic genetic construct to the target gene.

The genus of nucleotide sequences in the claimed synthetic genes is defined by the metes and bounds of the claim, based on the description in the specification. Applicants respectfully submit that the person of ordinary skill in the art would readily conclude that the genus claimed was contemplated by Applicants in the application. M.P.E.P. § 2164.01 provides that "[a] patent need not teach, and preferably omits, what is well known in the art" (citations omitted). Viral genes of single-stranded (+) RNA viruses and other target genes of animal cells are well known in the art, as are methods of obtaining nucleotide sequences of such genes. It is unreasonable for Applicants to list every known gene that could be a target by the claimed method. Such is unnecessary because one of skill in the art would readily envision each and every nucleotide sequence of Applicants' claimed invention upon selecting a desired gene to target based on the description in the specification. The application, when combined with no more than general knowledge in the art, describe the claimed invention in such a manner that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention, as required by M.P.E.P. § 2163.

The Examiner acknowledges that the specification describes what is encompassed by

substantial identity to a portion of a selected target gene and what is encompassed by a portion of a selected target gene. Exemplary target genes are presented, as noted at pages 10-11, and there is no requirement to list every target gene. The detailed description of the constructs is exemplified by the multiple drawings, particularly 13-15 and 19-20.

One of skill in the art at the time the invention was made would therefore recognize that Applicants were in possession of the claimed invention as presently claimed. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the objection under 35 U.S.C. § 112, first paragraph.

5. Claim Rejections Under 35 U.S.C. § 102(e)

Rejection Under 35 U.S.C. § 102(e) – Anticipation of claims 66, 67, 68, 69, 72, 73, 74, 82, 115, 117-119, 121, 123-125, 128, 130-139, 141, 143, 145, 147, 148, 149, 152 and 154-162

The Examiner rejected Claims 66, 67, 68, 69, 72, 73, 74, 82, 115, 117-119, 121, 123-125, 128, 130-139, 141, 143, 145, 147, 148, 149, 152, and 154-162 under 35 U.S.C. § 102(e) as being anticipated by Fire *et al.*, (U.S. 6,506,559) ("Fire"). The Examiner asserted that Fire teaches a vector comprising a construct comprising a promoter operably linked to a nucleotide sequence comprising dsRNA comprising a sense strand and an antisense strand of the target gene (columns 4 and 9), the dsRNA may be formed by a single self-complementary RNA strand or two complementary RNA strands (column 7), the construct. comprises a regulatory region including polyadenylation (columns 8-9), the nucleotide sequence may be at least 25 or 50 bases (column 8), the vector can be introduced into a cancerous cell, including cancer cells find in humans (columns 9-10), a viral vector or lipid mediated carrier transport can be used as the vector (column 9), the cell can comprise a target gene at risk from a pathogen including HIV or can be from several different types of animals (columns 4,

8, and 10), and the construct can comprise a structural gene with an intron. The Examiner further asserted that the structural gene can comprise a 5' or 3' untranslated region (column 20), the structural gene can be less than 2.0 kilobases (Table 1 and Figure 1), and the structural gene can comprise one or more strands of the nucleotide sequence (column 4).

Applicants' Response

Applicants respectfully traverse the rejection and request reconsideration based on the following comments.

To find anticipation under 35 U.S.C. § 102, every element of the claims must be taught in a single reference. M.P.E.P. § 2131; *See, e.g., Carella v. Starlight Archery and Pro Line Co.*, 804 F.2d 135, 138 (Fed. Cir. 1986). Applicants submit that Fire does not teach all of the elements of amended claims 66 and 67 and dependent claims, specifically at least the elements of i) two identical nucleotide sequences, ii) two identical nucleotide sequences oriented in a head-to-head, head-to-tail or tail-to-tail configuration, iii) a stuffer fragment, and iii) two identical nucleotide sequences placed under the control of separate promoter sequences. Fire does not teach a synthetic gene comprising two promoter sequences which are active in an animal cell.

It is important to note with respect to element i) above that "two identical nucleotide sequences" are not the same as "two complementary RNA strands" that Fire discloses in column 7, lines 43-44 and to which the Examiner has referred to in the statement of rejection. "Two complementary RNA strands" are by definition a sequence and its complement and are therefore not identical. The Examiner has not specified anywhere in Fire a disclosure of "two identical nucleotide sequences."

In relation to iii) above, Applicants note that the Examiner has acknowledged directly in the Office Action under the analysis of a rejection under 35 U.S.C. § 103 (a) that Fire does

not teach a stuffer fragment of 10-50 nucleotides in length. Office Action at page 13. Moreover, the Examiner makes use of Ladner as a secondary reference to provide the element of "stuffer fragment." Further, the Examiner has made the same acknowledgement of the lack of disclosure of a "stuffer fragment" in Fire in Office Actions issued in two other related patent applications. In an Office Action dated April 17, 2007, to Application Serial No. 10/346,853, the Examiner stated "Fire (and Jendrisak) do not specially teach a construct comprising structural gene sequences and a stuffer sequence separating the sequences." Office Action at page 21. Also, in an Office Action dated April 27, 2007, to Application Serial No. 10/646,070, the Examiner stated "Fire does not specifically teach separating a construct comprising the structural gene sequences with a stuffer sequence." Office Action at page 15.

To further prosecution of this application, Applicants have cancelled claims 75, 76, 79, 80, 129, 132, 133, 153, 156 and 157. Thus, the rejection related to those claims is moot.

Clearly, Fire does not teach each and every element of claims 66 and 67 or the arrangement of those elements as recited in the claim. Applicants have added new claims 163-171, which incorporate all of the limitations of amended claim 66. Therefore, Fire does not anticipate the newly presented claims. Fire does not anticipate the present invention.

Further, Applicants maintain that Fire is not a valid prior art reference under 35 U.S.C. § 102 in regard to the subject application. Applicants note that the effective filing date of the subject application for the material claimed is March 20, 1998. Fire issued from an application filed December 18, 1998, *i.e.*, after the first effective filing date of the subject application.

Fire claims the benefit of U.S. Provisional Application No. 60/068,562, filed December 23, 1997 (the "Fire Provisional"). The Fire Provisional, however, discloses less

than the Fire patent. Any rejection under 35 U.S.C. § 102 (e) can only be based on the disclosure of the Fire Provisional, not on the disclosure of the Fire patent. Applicants point out that the Fire Provisional discloses less than Fire, and therefore cannot disclose at least each of the elements i) two identical nucleotide sequences each substantially identical to a target gene in an animal cell, ii) two identical nucleotide sequences oriented in a head-to-head, head-to-tail or tail-to-tail configuration, and iii) two identical nucleotide sequences separated and linked by a stuffer fragment, in addition to further elements recited in the dependent claims of the instant application.

Finally, Applicants respectfully point out that the claimed invention was invented before the filing date of Fire, and before the filing date of the Fire Provisional. Applicants attach hereto as **Exhibit B and Exhibit C** copies of Declarations under 37 C.F.R. § 1.131 submitted in connection with U.S. Reexamination No. 90/007,247, the re-examination of the patent that issued from the '812 Application. As indicated in the declarations and accompanying exhibits, Applicants' invention was prior to the filing of the Fire Provisional. Fire is thereby removed as an effective prior art reference.

Applicants submit that Fire does not anticipate the claimed invention and respectfully request withdrawal of the rejection of under 35 U.S.C. § 102 (e).

6. Rejections Under 35 U.S.C. § 103(a)

The Examiner rejected dependent claims 68, 116, 126, 127, 138, 139, 140, 150, 151 and 153 under 35 U.S.C. 103(a) as being unpatentable over Fire et al (U.S. 6,506,559) ("Fire") taken with other references, specifically:

> claims 68, 126, 138, and 150 were rejected as being unpatentable over Fire taken with Ladner *et al.* (U.S. 5,198,346) ("Ladner");

claims 68, 127, 138, and 151 were rejected as being unpatentable over Fire taken with German *et al.* (U.S. 6,225,290) ("German");

claims 68, 116, 139, 140 were rejected as being unpatentable over Fire taken with Cowsert *et al.* (U.S. 5,580,767) ("Cowsert"); and

claims 68, 129, 139, and 153 were rejected as being unpatentable over Fire taken with Gengenbach (U.S. 6,069,298) (Gengenbach).

The Examiner asserted that Fire teaches a vector comprising a construct comprising a promoter operably linked to a nucleotide sequence comprising dsRNA comprising a sense strand and an antisense strand of the target gene (columns 4 and 9), the dsRNA may be formed by a single self-complementary RNA strand or two complementary RNA strands (column 7), the construct comprises a regulatory region including polyadenylation (columns 8-9), the nucleotide sequence may be at least 25 or 50 bases (column 8), the vector can be introduced into a cancerous cell, including cancer cells found in humans (columns 9-10), a viral vector or lipid mediated carrier transport can be used as the vector (column 9), the cell can comprise a target gene at risk from a pathogen including HIV or can be from several different types of animals (columns 4, 8, and 10), the target gene can be an endogenous in a human cell (columns 4 and 10-11), the construct can comprise a structural gene with an intron. The Examiner further asserted that the structural gene can comprise a 5' or 3' .untranslated region (column 20), the structural gene can be less than 2.0 kilobases (Table 1 and Figure 1), and the structural gene can comprise one or more strands of the nucleotide sequence (column 4).

In levying an obviousness rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing that the prior art references, when combined, teach or suggest all the claim limitations. M.P.E.P. §2143; *see also, In re Royka*, 490 F.2d 981 (C.C.P.A. 1974). To

determine obviousness, Examiners must consider (1) the scope and content of the prior art, (2) the differences between the claimed invention and the prior art, (3) the level of ordinary skill in the pertinent art, and (4) objective evidence relevant to the issue of obviousness." *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). In addition, the Supreme Court has noted that there must be a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the new invention does. *KSR International Co. v. Teleflex Inc.*, 550 U.S. __, 82 USPQ2d 1385 (2007). Here, the Examiner has not met the burden of showing obviousness.

Rejections of Claims 68, 126, 138 and 150 as Obvious over Fire with Ladner *et al.* (US 5,198,346)

The Examiner rejected claims 68, 126, 138, and 150 under 35 U.S.C. § 103(a) as being unpatentable over Fire taken with Ladner. The Examiner acknowledged that Fire does not specifically teach a construct comprising the structural gene sequences with a stuffer sequence of nucleotides 10-50 nucleotides in length. The Examiner asserted, however, that Ladner teaches using a stuffer fragment having above about 10 nucleotides to introduce a stop codon or a unique restriction site (column136 and Table 704), and teaches using a transcription termination sequence and a promoter to regulate transcription of the gene (column 136).

Applicants' Response

Applicants respectfully traverse the rejection.

As noted above, Applicants point out that Fire is not prior art against the subject application and this rejection is defective based on this threshold issue.

Further, Fire does not teach all the elements of the present invention in claims 66 and 67 or dependent claims 68, 126, 138 or 150. Specifically, Applicants maintain that 1) "the

synthetic genetic construct comprises two identical nucleotide sequences," 2) the two identical nucleotide sequences "oriented in a head-to-head, head-to-tail, or tail-to-tail configuration", 3) identical nucleotide sequences spatially separated and linked by a "stuffer fragment"; and 4) "the two identical nucleotide sequences substantially identical to the target gene" are not taught by the references. The genetic constructs of claims 68 and 138 include a stuffer fragment which spatially separates and links the two identical nucleotide sequences and which are under the control of a single promoter sequence, but do not provide a specific length limitation.

It is important to note with respect to element 1) above that "two identical nucleotide sequences" are not the same as "two complementary RNA strands" that Fire discloses in column 7, lines 43-44 and to which the Examiner has referred to in the statement of rejection. "Two complementary RNA strands" are by definition a sequence and its complement and are therefore not identical.

Additional art to incorporate the dependent limitations would not render obvious dependent claims.

Furthermore, the deficiencies of Fire are not cured by Ladner for the elements listed above or a length limitation of a stuffer fragment as in claims 126 and 150. Ladner teaches using a transcription termination sequence and a promoter to regulate transcription of the gene (column 136). The Examiner states that Ladner teaches a "stuffer fragment having about 10 nucleotides to introduce a stop codon or a unique restriction site. (column 136 and Table 704)." In response, Applicants submit that Ladner does not disclose "stuffer fragment having about 10 nucleotides." The linker sequence of Ladner, detailed in Table 704, does not correspond to the limitation recited in amended claims 126 and 150, namely a stuffer fragment is a sequence of nucleotides 10-50, 50-100, or 100-500 nucleotides in length which

spatially separates and links two identical nucleotide sequences, each of which is substantially identical to an animal target gene.

Ladner describes the generation of DNA-binding proteins obtained by variation of genes producing known binding proteins, and production and selection of these proteins in prokaryotic cells. Ladner does not contemplate use of dsRNA genetic constructs in animal cells, as taught by Applicants' presently claimed invention. Indeed, Ladner is about production (overexpression) of DNA-binding proteins, not down-regulation of gene expression. Ladner also is about production of proteins in prokaryotic cells, not eukaryotic animal cells. The Examiner's assertions that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire taken with Ladner to produce a construct comprising a structural gene with a stuffer sequence or an isolated animal cell comprising the construct are incorrect. One of ordinary skill in the art would not be motivated to combine the teachings of production of DNA binding proteins in prokaryotic cells to the use of dsRNA inhibition of gene expression in animal cells. Applicants respectfully submit that the combination of these two references is therefore inappropriate. Indeed, the references actually teach away from each other.

Most importantly, there is no technical basis from which one of skill in the art could have expected that modifying Fire as recited to include a stuffer fragment would have been successful. Certainly the teachings of Ladner relating to DNA binding proteins produced in prokaryotic cells do not offer the technical basis; Fire do not suggest that their technology could include a stuffer fragment between two identical sequences, let alone any advantage in doing so; and the April 25, 2007, Office Action offers no technical basis for concluding that one of skill would expect success in including a stuffer fragment. Absent such a technical

basis, an obviousness rejection cannot be proper. *KSR Int'l v. Teleflex, Inc.*, 550 U.S. ___ (2007).

Accordingly, Applicants maintain that each of claims 68, 126, 138 and 150 is patentable over Fire taken with Ladner, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Finally, as detailed above, Applicants respectfully point out that the claimed invention was invented before the filing date of Fire, and before the filing date of the Fire Provisional. As indicated in the Declarations, Applicants invented their invention prior to the filing of the Fire Provisional.

Rejections of Claims 68, 127, 138 and 151 as Obvious over Fire with German *et al.*, (US 6,225,290)

The Examiner rejected claims 68, 127, 138, and 151 under 35 U.S.C. § 103(a) as being unpatentable over Fire taken with German. The Examiner acknowledged that Fire does not specifically teach separating a construct comprising the structural gene sequences with a stuffer sequence comprising an intron, wherein the stuffer sequence spatially separates the gene sequences. The Examiner alleged that in view of the breadth of the term "two copies are spatially separated by a stuffer fragment which comprises an intron" the term reads on the stuffer being located between the two sequences including the stuffer being located before the first structural gene in a circular plasmid.

The Examiner asserted that German teaches that including one or more introns in a construct can increase the level of expression of a DNA of interest in the construct (columns 7-8), and teaches inserting the intron into the construct at a 5' position to the DNA of interest (column 8).

Applicants' Response

Applicants respectfully traverse the rejection.

As noted above, Applicants point out that Fire is not prior art against the subject application and this rejection is defective based on this threshold issue.

Further, Fire does not teach all the elements of the present invention in claims 66 and 67, let alone dependent claims 68, 127, 138 and 151. Specifically, Applicants maintain that at least 1) "the synthetic genetic construct comprises two identical nucleotide sequences," 2) the two identical nucleotide sequences "oriented in a head-to-head, head-to-tail, or tail-to-tail configuration", 3) identical nucleotide sequences spatially separated and linked by a "stuffer fragment"; and 4) "the two identical nucleotide sequences substantially identical to the target gene" are not taught by the references. The genetic constructs of claims 66, 67, 68 and 138 include a stuffer fragment which spatially separates and links the two identical nucleotide sequences and which are under the control of a single promoter sequence, but do not recite that the stuffer is an intron sequence.

It is important to note with respect to element 1) above that "two identical nucleotide sequences" are not the same as "two complementary RNA strands" that Fire discloses in column 7, lines 43-44 and to which the Examiner has referred to in the statement of rejection. "Two complementary RNA strands" are by definition a sequence and its complement and are therefore not identical.

Applicants note Examiner's comment that "(I)n view of the breadth of the term "two copies are spatially separated by a stuffer fragment which comprises an intron" the term reads on the stuffer being located between the two sequences including the stuffer being located before the first structural gene in a circular plasmid." (page 15). In response, Applicants point out that amended claim 66 recites that the two identical nucleotide sequences are i) spatially separated and linked by a stuffer fragment and ii) the identical nucleotides sequences and

stuffer fragment are placed operably under the control of a single promoter sequence and transcription termination sequence. The presence of a stuffer fragment **before** (5') the first structural gene in a circular plasmid does not meet these requirements.

Applicants note that claims 66 and 67, and rejected claims 68 and 138, do not recite an intron. Moreover, the deficiencies of Fire are not cured by German related to the limitation where the stuffer fragment is an intron sequence. German teaches constructs that may include an intron to enhance expression of a DNA of interest encoding a protein. German is about overexpression of DNA sequences to increase protein production, not down-regulation of gene expression. No where does German teach two identical nucleic acid sequences separated by an intron. General description of a known technique to include an intron in a construct does not teach the specific element of using an intron between identical nucleic acid sequences in a synthetic genetic construct to inhibit expression of a target gene. German does not teach two identical nucleotide sequences spatially separated and linked by a stuffer fragment that is an intron, wherein the identical nucleotide sequences and stuffer fragment are under the control of a single promoter and a transcription termination sequence. One of ordinary skill in the art would not be motivated to combine the teachings of production of DNA constructs to enhance production of proteins with the use of dsRNA for inhibition of gene expression in animal cells.

The genetic constructs comprising the two identical nucleotide sequences linked with an intron of the present invention provide enhanced *inhibition* of genetic expression. Levin *et al.*, *Plant Molecular Biology* 44:759-775 (2000), demonstrate superior results using nucleotide sequences with a stuffer fragment, reporting that expression of a transcript with a spacer or stuffer fragment between the sense and antisense sequence "led to stronger

inactivation" of a gene than did "constructs with a minimal spacing between the sense and antisense fragments," see Abstract, lines 9-11; see also pg. 768, Figure 5.

Similarly, Smith *et al.*, *Nature* 407:319-320 (2000) discloses that using a stuffer fragment not only led to stability of the nucleic acid construct (*see, e.g.*, pg. 320, col. 1 ll. 25-29; see also *id.* at ll. 32-35), but that certain stuffer fragments lead to up to 100% inhibition of the target gene expression. *See, e.g.*, first paragraph and Figure 1. These references provide evidence of the advantageous properties of the genetic constructs with a stuffer fragment in inhibiting gene expression.

Applicants respectfully submit that the combination of these two references is therefore suspect.

Most importantly, there is no technical basis from which one of skill in the art could have expected that modifying either reference to include a stuffer fragment which is an intron sequence would have been successful. Certainly the teachings of German relating to protein production in prokaryotic cells do not offer the technical basis; Fire do not suggest that their technology could include a stuffer fragment between two identical sequences, let alone any advantage in doing so where the stuffer fragment is an intron sequence; and the April 25, 2007 Office Action offers no technical basis for concluding that one of skill would expect success in including a stuffer fragment which is an intron sequence. Absent such a technical basis, an obviousness rejection cannot be proper. *KSR Int'l v. Teleflex, Inc.*, 550 U.S. ___ (2007).

Accordingly, Applicants maintain that each of claims 68, 127, 138 and 151 is patentable over Fire taken with German and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Finally, as detailed above, Applicants respectfully point out that the claimed invention was invented before the filing date of Fire, and before the filing date of the Fire Provisional. As indicated in the Declarations, Applicants invented their invention prior to the filing of the Fire Provisional. This reference is therefore removed as prior art.

Rejections of Claims 68, 116, 139 and 140 as Obvious over Fire with Cowsert *et al.* (US 6,506,559)

The Examiner rejected claims 68, 116, 139, 140 under 35 U.S.C. § 103(a) as being unpatentable over Fire taken with Cowsert. The Examiner acknowledged that Fire does not specifically teach targeting RNA polymerase of a viral gene. The Examiner asserted that Cowsert teaches antisense for inhibiting RNA polymerase (column 3).

Applicants' Response

Applicants respectfully traverse the rejection.

As noted above, applicants point out that Fire is not prior art against the subject application and this rejection is defective based on this threshold issue.

Fire does not teach all the elements of the present invention in claims 66 and 67 let alone dependent claims 68, 116, 139 and 140. Specifically, Applicants maintain that at least 1) "the synthetic genetic construct comprises two identical nucleotide sequences," 2) the two identical nucleotide sequences "oriented in a head-to-head, head-to-tail, or tail-to-tail configuration", 3) identical nucleotide sequences spatially separated and linked by a "stuffer fragment"; and 4) "the two identical nucleotide sequences substantially identical to the target gene" are not taught by the references. The genetic constructs of claims 66, 67 and 68 include a stuffer fragment which spatially separates and links the two identical nucleotide sequences and which are under the control of a single promoter sequence, but do not recite that the target gene is a viral gene.

It is important to note with respect to element 1) above that "two identical nucleotide sequences" are not the same as "two complementary RNA strands" that Fire discloses in column 7, lines 43-44 and to which the Examiner has referred to in the statement of rejection. "Two complementary RNA strands" are by definition a sequence and its complement and are therefore not identical.

Cowsert does not cure the deficiencies of Fire. Cowsert is directed to antisense oligonucleotides for inhibiting viral RNA. Cowsert describes use of oligonucleotides, not genetic constructs, for inhibiting genes encoding RNA polymerase. Nowhere does Cowsert contemplate a genetic construct with two identical nucleotide sequences linked by a stuffer fragment, under the control of a single promoter and transcription termination sequence, that can inhibit the genetic expression of the gene. Cowsert is non-analogous art to interfering RNA. Fire itself claims its dsRNA is different and distinct to antisense sequences, and improvement over antisense: "The present invention differs from antisense-mediated interference in both approach and effectiveness." Fire, column 3, lines 19-20. One of skill in the art would not be motivated to combine the teachings of antisense oligonucleotides of Cowsert with the dsRNA of Fire to use a synthetic genetic construct according to claims 66 and 67 and the depending claims. It would not have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Fire and Cowsert, to produce a synthetic genetic construct with two identical nucleotide sequences separated by a stuffer fragment or an isolated animal cell comprising the construct, particularly when neither references teaches those elements. Applicants respectfully submit that the combination of these two references is therefore suspect.

Accordingly, Applicants maintain that each of claims 68, 116, 139 and 140 is patentable over Fire taken with Cowsert, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Finally, as detailed above, applicants respectfully point out that the claimed invention was invented before the filing date of Fire, and before the filing date of the Fire Provisional. As indicated in the Declarations, applicants invented their invention prior to the filing of The Fire Provisional. This reference is therefore removed as prior art.

Rejections of Claims 68, 129, 139, and 153 as Obvious over Fire with Gengenbach (US 6,506,559)

The Examiner rejected claims 68, 129, 139, and 153 under 35 U.S.C. § 103(a) as being unpatentable over Fire taken with Gengenbach. The Examiner acknowledged that Fire does not specifically teach the structural gene is no more than 0.5 kilobases (kb). The Examiner asserted, however, that Gengenbach teaches antisense to an about 0.5 kb region of the maize ACCase cDNA that has high homology to the chicken ACCase gene (column 37).

Applicants' Response

Applicants respectfully traverse the rejection.

As noted above, Applicants point out that Fire is not prior art against the subject application and this rejection is defective based on this threshold issue.

Further, Fire does not teach all the elements of the present invention in claims 66 and 67 or dependent claims 68, 129, 139 and 153. Specifically, Applicants maintain that at least 1) "the synthetic genetic construct comprises two identical nucleotide sequences," 2) the two identical nucleotide sequences "oriented in a head-to-head, head-to-tail, or tail-to-tail configuration", 3) identical nucleotide sequences spatially separated and linked by a "stuffer fragment"; and 4) "the two identical nucleotide sequences substantially identical to the target

gene" are not taught by the references. The genetic constructs of claims 66, 67 and 68 include a stuffer fragment which spatially separates and links the two identical nucleotide sequences and which are under the control of a single promoter sequence, but do not recite that the target gene is a viral gene.

It is important to note with respect to element 1) above that "two identical nucleotide sequences" are not the same as "two complementary RNA strands" that Fire discloses in column 7, lines 43-44 and to which the Examiner has referred to in the statement of rejection. "Two complementary RNA strands" are by definition a sequence and its complement and are therefore not identical.

Applicants note that rejected claims 68 and 139 do not contain the limitation of the nucleotide sequence length of no more than 0.5-2.0 kilobases. The deficiencies of Fire are not cured by Gengenbach. Applicants have cancelled claims 129 and 153, thereby rendering the rejection to those claims moot.

Amended claims 128 and 152 recite that the **total** length of the identical nucleotide sequences is no more than 0.5-2.0 kilobases. Applicants submit that Gengenbach does not teach that the total length of two identical nucleotide sequences is no more than 0.5-2.0 kilobases. Gengenbach does not even disclose two identical nucleotide sequences. The specific disclosure that the Examiner refers to in Gengenbach relates to an expression system that can be used to screen antisense DNA sequences against maize ACCase. "For example, an antisense sequence can be obtained that is complementary to an about 0.5 kb region of the maize ACCase cDNA that has high homology with a portion of a chicken ACCase gene...." The specific length being referred to in Gengenbach is not the length of the antisense sequence but rather the length of the homologous region between the maize and chicken ACCase genes.

Not only do the references not teach or suggest all of the elements of the present invention, they are nonanalogous art that one of ordinary skill in the art would not be motivated to combine. Applicants respectfully submit that the combination of these two references is suspect.

Most importantly, there is no technical basis from which one of skill in the art could have expected that modifying either reference to include two identical nucleotide sequences with a total length of no more than 0.5-2.0kb would have been successful. Certainly the teachings of Gengenbach directed to maize ACCase and its homology with chicken ACCase do not offer the technical basis; Fire do not suggest that their technology could include two identical nucleotide sequences with a total length of no more than 0.5-2.0kb, let alone any advantage in doing so; and the April 25, 2007 Office Action offers no technical basis for concluding that one of skill would expect success in including a stuffer fragment which is an intron sequence. Absent such a technical basis, an obviousness rejection cannot be proper. *KSR Int'l v. Teleflex, Inc.*, 550 U.S. ___ (2007).

Applicants point to the disclosure in the present application page 17, lines 8 to 22 which refer to the advantage of the total length being no more than 0.5-2.0kb in reducing the instability of repeated nucleotide sequences and minimizing recombination events. Such advantage is not taught or suggested in either Fire or Gengenbach.

Accordingly, Applicants maintain that each of claims 68, 129, 139 and 153 is patentable over Fire taken with Gengenbach, and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Finally, as detailed above, applicants respectfully point out that the claimed invention was invented before the filing date of Fire, and before the filing date of the Fire Provisional.

As indicated in the Declarations, applicants invented their invention prior to the filing of the Fire Provisional. This reference is therefore removed as prior art.

7. **Double Patenting**

Non-statutory Obviousness-type Double Patenting Rejection over U.S. Patent No. 6,573,099

The Examiner has rejected claims 66, 67, 68, 69, 72-74, 82, 123-138, and 147-162 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 11-15 and 19-21 of the '099 patent. The Examiner notes that the conflicting claims are not identical, but asserted they are not patentably distinct from each other because both set of claims are directed to a dsRNA construct.

In the present application, Applicants have amended independent claims 66 and 67 and the depending claims to direct a synthetic genetic construct comprising two identical nucleotide sequences each of which is substantially identical to a target gene in an animal cell, wherein the two identical nucleotide sequences are oriented in a head-to-head, head-to-tail or tail-to-tail configuration relative to each other and are spatially separated and linked by a stuffer fragment which comprises nucleotides. The two identical nucleotide sequences and stuffer fragment are placed operably under the control of a single promoter sequence or two separate promoters, which are operable in the cell, and a transcription termination sequence which is active in the cell.

In addition, Applicants note that the '099 patent is currently in reexamination, U.S. Serial No. 90/007,247, which is merged with a second reexamination of the patent, U.S. Serial No. 90/008,096. Currently in the reexamination, claims 1-3 and 8-9 have been cancelled and claims 4-6 and 10-18 have been amended.

Applicants submit that the amended claims of the present invention are patentably distinct over the amended claims of the '099 patent in reexamination and eliminate any consideration of double-patenting issues. Nevertheless, Applicants respectfully request the rejection be held in abeyance pending indication of allowable subject matter in the instant application and resolution of the reexamination of the '099 patent.

Provisional Non-statutory Obviousness-type Double Patenting Rejection Rejections Over Pending Claims in US Patent Applications

The Examiner provisionally rejected claims 66, 67, 68, 69, 72-74, 82, 123-138, and 147-162 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 56, 59,60,62,63,65-67, 77-101, and 107 of co-pending Application No. 09/646,807. The Examiner asserted that although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims read on a dsRNA construct for reducing expression of a target gene in an animal cell.

The Examiner provisionally rejected claims 66, 67, 68, 69, 72-74, 82, 123-138, and 147-162 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 34, 66, 78, 79, of co-pending Application No. 10/346,853. The Examiner asserted that although the conflicting claims are not identical, they are not patentably distinct from each other because both set of claims read on a dsRNA construct for reducing expression of a target gene in an animal cell.

The Examiner provisionally rejected claims 66, 67, 68, 69, 72-74, 82, 123-138, and 147-162 on the ground of nonstatutory obviousness type double patenting as being unpatentable over claims 46, 47,59-61,66-70, and 74-80 of co-pending Application No. 11/180,928. The Examiner asserted that although the conflicting claims are not identical,

they are not patentably distinct from each other because both set of claims read on a dsRNA construct for reducing expression of a target gene in an animal cell.

The Examiner noted that these are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented. Applicants submit that the claims in each of these applications are patentably distinct from the present invention. Nevertheless, Applicants respectfully request the rejections be held in abeyance pending indication of allowable subject matter in the applications.

Disclosure of Co-pending Patent Applications

The Examiner noted that there "at least five other" co-pending applications that might have claims embracing the subject matter of the claimed invention. Office Action at page 20. The Examiner reminded Applicants of their duty to disclose any pending applications or patents containing claims that read on the claimed invention, which are not listed above, under 37 CFR § 1.56.

Applicants submit that there are four other co-pending patent applications with the present application not listed above that all claim priority to the '099 patent. Applicants have disclosed all of the co-pending applications in Information Disclosure Statements filed in each of these patent applications.

In addition, Applicants bring to the Examiners attention four other pending patent applications that are commonly owned by the owner of the subject application and have overlapping inventors, specifically:

US Application No. 09/287632, U.S. Publication No. 2004-0214330

US Application No. 11/364183, U.S. Publication No. 2006-0178335

US Application No. 11607062, U.S. Publication No. 2007-0078105

US Application No. 11/841737.

Applicants will bring to the attention of the Office any other related applications that may be filed in the future in accordance with their duty of disclosure.

Disclosure of Prior or Concurrent Proceedings

Applicants duly inform the Examiner of the ruling of the U.S. Court of Appeals for the Federal Circuit (CAFC) to the appeal of the U.S. District Court of Delaware's decision in *Benitec Australia, Ltd. v. Nucleonics, Ltd.*, No. 04-0174 (D. Del. September 29, 2005) (order granting Benitec's Motion for Voluntary Dismissal Without Prejudice). The CAFC affirmed the ruling of the District Court in granting Benitec's motion to dismiss. *Benitec Australia, Ltd. v. Nucleonics, Ltd.*, No. 06-1122 (Fed. Cir. July 20, 2007). This litigation involves a claim of patent infringement of Patent No. U.S. Patent No. 6,573,099. Benitec is a co-assignee of the '099 patent with the CSIRO, the assignee of the subject application. On October 11, 2007, the CAFC denied a Petition for Rehearing and Rehearing *En Banc* filed by the defendant/appellant Nucleonics, Inc.

In addition, in an appeal hearing of the Technical Board of Appeal of the European Patent Office (EPO) on April 24, 2007, regarding a European patent application related to the '099 patent (EP1071762), the EPO rejected the patent application for formal technical reasons unrelated to substantive enablement or obviousness issues. (Appeal No. T1491/05-3308). In the United States, amendments may be made to applications at any time, while it is our understanding that such amendments are not available in European practice, and the formal technicalities affecting the European application would not have arisen under United States rules. The claims are being pursued in Europe in divisional applications.

8. Conclusion

In view of the above amendments, Applicants believe the pending application is in condition for allowance.

Applicants submit concurrently a request for a three-month extension of time under 37 C.F.R. 1.136 and the accompanying fee. Please charge our Credit Card in the amount of $1,050.00 covering the fee set forth in 37 C.F.R. § 1.136(a). Credit Card Payment Form SB-2038, with a signature from an authorized cardholder, is enclosed. In the event that any additional extension of time is necessary to prevent the abandonment of this patent application, then such extension of time is petitioned. The U.S. Patent and Trademark Office is authorized to charge any additional fees that may be required in conjunction with this submission to Deposit Account Number 50-2228, from which the undersigned is authorized to draw.

Dated: October 25, 2007

Respectfully submitted,

By _____

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EXHIBIT A